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16568

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	HELMUT H. MROZIK	
Serial No.	:	358,736 - Case 16568	Art Unit:
Filed	:	3-16-82	Examiner:
For	:	4"-KETO-AND 4"-AMINO-4"-DEOXY AVERMECTIN COMPOUNDS AND SUBSTITUTED AMINO DERIVATIVES THEREOF	

Commissioner of Patents and Trademarks
Washington, D. C. 20231

DISCUSSION OF PRIOR ART UNDER 35 C.F.R. 1.97

The following references may be of interest to the Examiner in the examination of the above-identified application.

U.S. Patents 4,310,519 to Albers-Schonberg et al.

4,199,569 to Chabala et al.

4,206,205 to Mrozik et al.

4,098,993 to Bright (I).

4,090,017 to Sciavolino (I).

4,133,950 to Myers (I).

4,085,119 to Myers (II).

Chemical Abstracts 91:175223f to Bright (II).

90:23614a to Sciavolino (II).

90:23615b to Sciavolino (III).

Copies of the foregoing references are enclosed herewith for the convenience of the Examiner.

REMARKS

The instant invention is concerned with derivatives of avermectin compounds wherein the hydroxy and the 4' or 4" position is oxidized to a keto and subsequently substituted by amino or substituted amino. The foregoing references disclose either avermectin compounds which have not had the foregoing reactions carried out thereon or other compounds substituted with an oleandrose group which have had various reactions carried out thereon.

Albers-Schonberg et al. which is cited in the instant application on page 1, line 12 disclose the avermectin compounds as prepared from the fermentation broth of streptomyces avermitilis. The avermectin compounds are substituted by a disaccharide group specifically the α-L oleandrose α-L oleandrosal group. There is no suggestion however that the 4" position hydroxy group can be converted to any other group.

Chabala et al. disclose avermectin compounds wherein the 22, 23 double bond had been reduced to a single bond. There is no suggestion of any reactions at the 4" position.

Mrozik et al. disclose avermectin compounds wherein one or both of the α L-oleandrose groups has been removed. No replacement or substitution reactions at the 4' or 4" positions is suggested.

The foregoing three references disclose the starting materials for the preparation of the instant compounds.

Bright et al. disclose the antibiotic oleandomycin and derivatives thereof. The oleandomycin substrate is noticed as being considerably different from the instant avermectin substrate; however, the substrate is substituted by oleandrose groups which are variously substituted including amine and substituted amine groups.

Sciavolino (I) discloses also oleandomycin compounds wherein the oleandrose substituent has been substituted with amino groups.

Myers (I) discloses similar compounds to Bright (I) and Sciavolino (I), however, it is noted that the oleandrosyl substitutent group is substituted with a complex substituted alkoxy carbonyl amino group.

Similarly Myers (II) discloses oleandomycin substituents containing a complex substituted alkyl group. Bright (II) discloses oleandomycin compound substituted at the oleandrocyl amino groups with substitutent groups such as the benzyloxycarbonyl.

Sciavolino (II) and (III) disclose compounds wherein the oleandrosyl group at the 4-position is disubstituted with various oxygen and nitrogen containing groups.

The foregoing various Bright, Sciavolino and Myers references disclose generally oleandrosyl containing compounds, however, there is no suggestion of the instant avermectin compounds containing the disaccharide α-L oleandrose α-L oleandrosyl group and no suggestion is made

that the instant 4' and 4" keto and amino groups could be prepared. Applicant's attorney respectfully submits that the foregoing references disclose the state of the art and that such references do not anticipate or render obvious the instant claims. The instant claims being allowable a prompt Notice of Allowance is respectfully solicited.

Respectfully submitted,

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Date: May 12, 1982
ENCLOSURES

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on the date appearing below.

MERCK & CO., INC.

By David C. Rose Date 12 May 1982